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| 10/734,024 | 12/11/2003 | David B. Weiner | UPVG0005-101 | 2356 |
| 34132 7590 02/20/2008 COZEN O'CONNOR, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508 | | | | |
| EXAMINER | | | | |
| HUMPHREY, LOUISE WANG ZHIYING | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/734,024

Applicant(s)

WEINER ET AL.

Examiner

LOUISE HUMPHREY

Art Unit

1648

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-23 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-23 and 32-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Response to Amendment

In view of the brief filed on November 30, 2007, PROSECUTION IS HEREBY REOPENED. See the rejections set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648.

Claims 1-20 and 24-31 have been cancelled. Claims 21-23 and 32-34 are pending and currently examined.

Claim Objections

Claim 21 is objected to because of the following informalities: the claim refers to the proteins Vpr by its acronym without first identifying it by the full name, HIV-1 viral protein R. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Applicant's arguments, see pages 11-16 and 20-24, filed on 30 November 2007 in the appeal brief, with respect to the rejection of claims 21-23 and 32-34 under 35 U.S.C. §103(a) as being unpatentable over Rogel *et al.* (February, 1995) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the different interpretation of the previously applied reference. See the new enablement rejection below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-5, 14, 15, 20, 25-27 and 29-34 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in response to Applicants' amendment.

New Rejection: Claims 21-23 and 32-34 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is the inhibition and prevention of lymphocyte activation by Vpr protein. The breadth of the claims encompasses both B lymphocytes and T lymphocytes and both *in vitro* and *in vivo* prevention and inhibition.

The disclosure fails to provide any working embodiments that meet the claimed limitations. While there are examples of assays to identify Rip-1-binding fragments of Vpr that are inducers or inhibitors of glucocorticoid receptor (GR) type II complex

translocation from cytoplasm to the nucleus, no *in vitro* or *in vivo* working example of any prevention or inhibition of lymphocyte activation is disclosed in the specification.

The specification provides no guidance regarding practice of the claimed methods. The specification refers generally to the Vpr's interaction with the glucocorticoid steroid biochemical pathway (page 22, line 26-37), that the expression of Vpr within the cell causes the cell to stop proliferating (page 5, line 31-35) and that Vpr inhibits cytokine production/secretion by T cells, B cells, and monocytes during immunoglobulin activation (page 10, lines 14-20). However, the disclosure is silent pertaining to specific method steps of inhibition and prevention of lymphocyte activation. The disclosure fails to provide any guidance pertaining to the structural characteristics or mechanisms of the interaction between Vpr and lymphocytes. The specification specifically discloses in more details and in working examples the use of Vpr or Rip-1-binding fragments of Vpr protein as transfection agent for the delivery of conjugated nucleic acid molecule or derivatives into the nucleus of a cell (page 36-37), which is not remotely related to inhibition or prevention of lymphocyte activation. Therefore, the disclosure does not correlate with the claimed method of preventing and inhibiting lymphocyte activation *in vitro* or *in vivo*, especially inside humans.

At the time the invention was made, successful implementation of lymphocyte activation inhibition and prevention with Vpr was not routinely practiced by those skilled in the art. Prior art only teaches T lymphocytes to secrete cytokines upon activation (Mosmann, 1997) and B lymphocytes to produce immunoglobulins once activated by cytokines (Paul, 1987). The only effect of Vpr expression within cells is the alteration of

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distribution of cells in the cell cycle and thereby mediating the prevention of cell proliferation (Rogel, February 1995). The prior art is unpredictable and fails to provide sufficient illumination pertaining to the mechanisms underlying inhibition and prevention of lymphocyte activation by the Vpr protein.

There is no specific guidance in the art or specification and no specific examples of the claimed method set forth in the specification. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to practice the claimed invention. Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). There is no evidence that Vpr has any effect on T lymphocyte secretion of cytokines, let alone the any effect on the activation of B lymphocytes. Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue and unpredictable experimentation from the skilled artisan to practice the claimed invention.

In conclusion, the instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LOUISE HUMPHREY whose telephone number is

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(571)272-5543. The examiner can normally be reached on Mon-Thu, 9:00 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./

Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648